Atty's Docket No.

1889-00401

Applicants: Dennis CVITKOVITCH, et al.

Title: Signal Peptides, Nucleic Acid Molecules and Methods for Treatment of Caries 09/833,017

Sheet 1 of 19

Figure 1

# Streptococcus mutans ComCDE Operon



Title: Signal Peptides, Nucleic Acid Molecules and Methods for

Treatment of Caries 09/833,017

Sheet 2 of 19

## Figure 2

#### Α.

[ATGAAAAAACACTATCATTAAAAAATGACTTTAAAGAAATTAAGACTGATGAATTAG AGATTATCATTGGCGGA (AGCGGAAGCCTATCAACATTTTTCCGGCTGTTTAACAGAAG TTTTACACAAGCTTTGGGAAAA)] TAA

B.  $\begin{center} AGCGGAAGCCTATCAACATTTTTCCGGCTGTTTAACAGAAGTTTTACACAAGCTTTGGG\\ AAAA \end{center} \label{eq:AAAA}$ 

C.

[ATGAATGAAGCCTTAATGATACTTTCAAATGGTTTATTAACTTATCTAACCGTTCTAT TTCTCTTGTTTCTATTTTCTAAGGTAAGTAATGTCACTTTATCGAAAAAGGAATTAACT CTTTTTTCGATAAGCAATTTTCTGATAATGATTGCTGTTACGATGGTGAACGTAAACCT GTTTTATCCTGCAGAGCCTCTTTATTTTATAGCTTTATCAATTTATCTTAATAGACAGA ATAGTCTTTCTCTAAATATTTTTATGGTCTGCCTGCTGCCAGTTCTGACTTGTTT AGGCGGCAATCATATTCTTTATCTTGGATGGAACTCAAGGAATTGTAATGGGCAGTAG CATTATAACCACCTATATGATCGAGTTTGCAGGAATAGCGCTAAGTTACCTCTTTCTCA GTGTGTTCAATGTTGATATTGGTCGACTTAAAGATAGTTTGACCAAGATGAAGGTCAAA AAACGCTTGATTCCAATGAATATTACTATGCTTCTATACTACCTTTTAATACAGGTATT GTATGTTATAGAGAGTTATAATGTGATACCGACTTTAAAATTTCGTAAATTTGTCGTTA TTGTCTATCTTATTTTTTTTTGATTCTGATCTCATTTTTAAGCCAATATACCAAACAA AAGGTTCAAAATGAGATAATGGCACAAAAGGAAGCTCAGATTCGAAATATCACCCAGTA TAGTCAGCAAATAGAATCTCTTTACAAGGATATTCGAAGTTTCCGCCATGATTATCTGA ATATTTTAACTAGCCTCAGATTAGGCATTGAAAATAAAGATTTAGCTAGTATTGAAAAG ATTTACCATCAAATCTTAGAAAAAACAGGACATCAATTGCAGGATACCCGTTATAATAT CGGCCATCTAGCTAATATTCAAAACGATGCTGTCAAGGGTATCTTGTCAGCAAAAATCT TAGAAGCTCAGAATAAAAAGATTGCTGTCAATGTAGAAGTCTCAAGTAAAATACAACTG  ${\tt CCTGAGATGGAGTTGCTTGATTTCATTACCATACTTTCTATCTTGTGTGATAATGCCAT}$ TGAGGCTGCTTTCGAATCATTAAATCCTGAAATTCAGTTAGCCTTTTTTAAGAAAAATG GCAGTATAGTCTTTATCATTCAGAATTCCACCAAAGAAAAACAAATAGATGTGAGTAAA ATTTTTAAAGAAACTATTCCACTAAAGGCTCCAATCGCGGTATTGGTTTAGCAAAGGT TATTCAAGCAACTCCTAATAATAAAA] TAG

D.
[ATGATTTCTATTTTTGTATTGGAAGATGATTTTTTACAACAAGGACGTCTTGAAACCA
CCATTGCAGCTATCATGAAAGAAAAAATTGGTCTTATAAAGAATTGACTATTTTTGGA
AAACCACAACAACTTATTGACGCTATCCCTGAAAAGGGCAATCACCAGATTTTCTTTT
GGATATTGAAATCAAAAAAAGAGGAAAAGAAGGACTGGAAGTAGCCAATCAGATTAGAC
AGCATAATCCTAGTGCAGTTATTGTCTTTGTCACGACACATTCTGAGTTTATGCCCCTC
ACTTTTCAGTATCAGGTATCTGCTTTGGATTTATTGATAAATCTTTGAATCCTGAGGA
GTTCTCCCACCGCATTGAATCAGCGCTGTATTATGCTATGGAAAACAGCCAGAAGAATG
GTCAATCAGAGGAACTTTTTATTTTCCATTCATCTGAAACTCAGTTTCAGGTCCCTTTT
GCTGAGATTCTGTATTTTGAAACATCTTCAACAGCCCATAAGCTCTGCCTTTATACTTA
TGATGAACGGATTGAATTCTACGGCAGTATGACTTGACATTGTTAAAATGGATAAGAGAC

Atty's Docket No. 1889-00401

Applicants: Dennis CVITKOVITCH, et al.

Title: Signal Peptides, Nucleic Acid Molecules and Methods for Treatment of Caries 09/833,017

Sheet 3 of 19

Figure 2 (cont'd)

 $\tt TTTTTCAGTGCCATCGCTCTTTTATTGTCAATCCTGCCAATATTACCCGTATTGATCGG$ AAAAAACGCTTGGCCTATTTTCGAAATAATAAGTCTTGTCTTATTTCACGAACTAAGTT AACAAAACTGAGAGCTGTGATTGCTGATCAAAGGAGAGCAAAA] TGA

Title: Signal Peptides, Nucleic Acid Molecules and Methods for

Treatment of Caries 09/833,017

Sheet 4 of 19

## Figure 3

- A. MKKTLSLKNDFKEIKTDELEIIIGGSGSLSTFFRLFNRSFTQALGK
- B.

  MNEALMILSNGLLTYLTVLFLLFLFSKVSNVTLSKKELTLFSISNFLIMIAVTMVNVNL
  FYPAEPLYFIALSIYLNRQNSLSLNIFYGLLPVASSDLFRRAIIFFILDGTQGIVMGSS
  IITTYMIEFAGIALSYLFLSVFNVDIGRLKDSLTKMKVKKRLIPMNITMLLYYLLIQVL
  YVIESYNVIPTLKFRKFVVIVYLILFLILISFLSQYTKQKVQNEIMAQKEAQIRNITQY
  SQQIESLYKDIRSFRHDYLNILTSLRLGIENKDLASIEKIYHQILEKTGHQLQDTRYNI
  GHLANIQNDAVKGILSAKILEAQNKKIAVNVEVSSKIQLPEMELLDFITILSILCDNAI
  EAAFESLNPEIQLAFFKKNGSIVFIIQNSTKEKQIDVSKIFKENYSTKGSNRGIGLAKV
  NHILEHYPKTSLQTSNHHHLFKQLLIIK
- C.
  MISIFVLEDDFLQQGRLETTIAAIMKEKNWSYKELTIFGKPQQLIDAIPEKGNHQIFFL
  DIEIKKEEKKGLEVANQIRQHNPSAVIVFVTTHSEFMPLTFQYQVSALDFIDKSLNPEE
  FSHRIESALYYAMENSQKNGQSEELFIFHSSETQFQVPFAEILYFETSSTAHKLCLYTY
  DERIEFYGSMTDIVKMDKRLFQCHRSFIVNPANITRIDRKKRLAYFRNNKSCLISRTKL
  TKLRAVIADQRRAK

Atty's Docket No. 1889-00401
Applicants: Dennis CVITKOVITCH, et al.
Title: Signal Peptides, Nucleic Acid Molecules and Methods for Treatment of Caries 09/833,017

Figure 4

Sheet 5 of 19

B. consensus: 1 MKKTLSLKNDFKEIKTDELEIIIGG SGSLSTFFRLFNRSFTQALGK 46 predicted cleavage site:

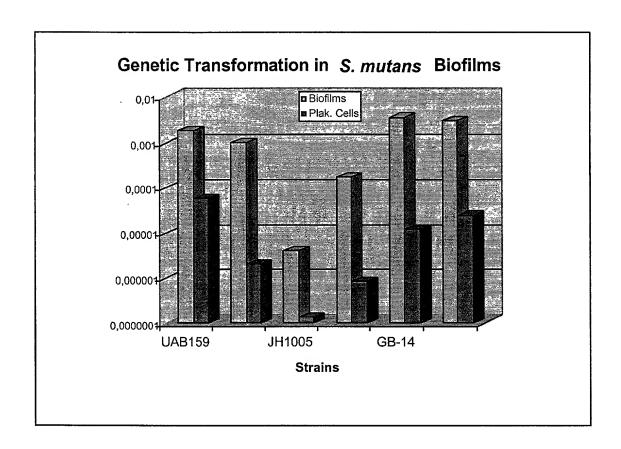
Figure 5

SGSLSTFFRLFNRSFTQALGK

Atty's Docket No. 1889-00401
Applicants: Dennis CVITKOVITCH, et al.
Title: Signal Peptides, Nucleic Acid Molecules and Methods for Treatment of Caries 09/833,017

Sheet 6 of 19

Figure 6



Title: Signal Peptides, Nucleic Acid Molecules and Methods for

Treatment of Caries 09/833,017

Sheet 7 of 19

Figure 7

Strain	Peptide added Number of Transformants/Recipients	No peptide Number of Transformants/Recipients
UAB15	4.65 X 10 <sup>-1</sup> 6.98 X 10 <sup>-2</sup>	1.78 X 10 <sup>-6</sup>
JH1005 <sup>2</sup>	6.98 X 10	V

The final concentration of SCSP used was 500 ng/ml.

The strain contains a nonsense mutation in the comC gene encoding the CSP.

1889-00401 Atty's Docket No. Applicants: Dennis CVITKOVITCH, et al.

Title: Signal Peptides, Nucleic Acid Molecules and Methods for Treatment of Caries 09/833,017

Sheet 8 of 19

# Figure 8

ComC region

ComC Primer Pair: F5-B5

[F5] 23406-23424 5'- AGTTTTTTGTCTGGCTGCG -3'

19 nt forward primer pct G+C: 47.4 Tm: 50.5

[B5] 24056-24037 5'- TCCACTAAAGGCTCCAATCG -3'

20 nt backward primer pct G+C: 50.0 Tm: 51.9

651 nt product for F5-B5 pair (23406-24056)

Optimal annealing temp: 50.3 pct G+C: 30.9 Tm: 71.5

ComD region

ComD Primer Pair: F1-B1

[F1] 392-415 5'- CGCTAAGTTACCTCTTTCTCAGTG -3' 24 nt forward primer pct G+C: 45.8 Tm: 51.6

> 683-663 5'- GCTTCCTTTTGTGCCATTATC -3' [B1] 21 nt backward primer pct G+C: 42.9 Tm: 50.8

> > 292 nt product for F1-B1 pair (392-683) Optimal annealing temp: 49.5 Tm: 70.2 pct G+C: 30.8

ComE region

ComE Primer Pair: F1-B1

[F1] 145-165 5'- CCTGAAAAGGGCAATCACCAG -3'

> 21 nt forward primer pct G+C: 52.4 Tm: 55.9

[B1] 606-585 5'- GCGATGGCACTGAAAAAGTCTC -3'

> 22 nt backward primer pct G+C: 50.0 Tm: 55.4

462 nt product for F1-B1 pair (145-606)

Optimal annealing temp: 53.6

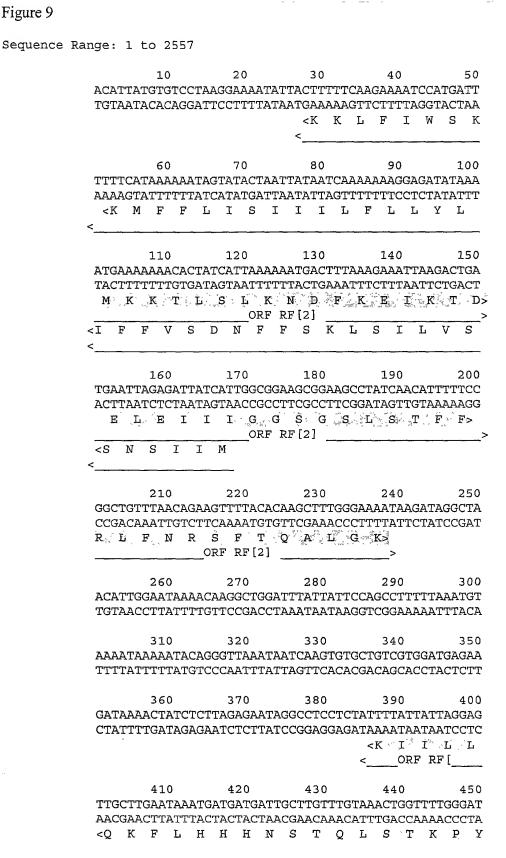
Tm: 74.1 pct G+C: 38.3

Signal Peptides, Nucleic Acid Molecules and Methods for

Treatment of Caries 09/833,0/7

Sheet 9 of 19

Figure 9

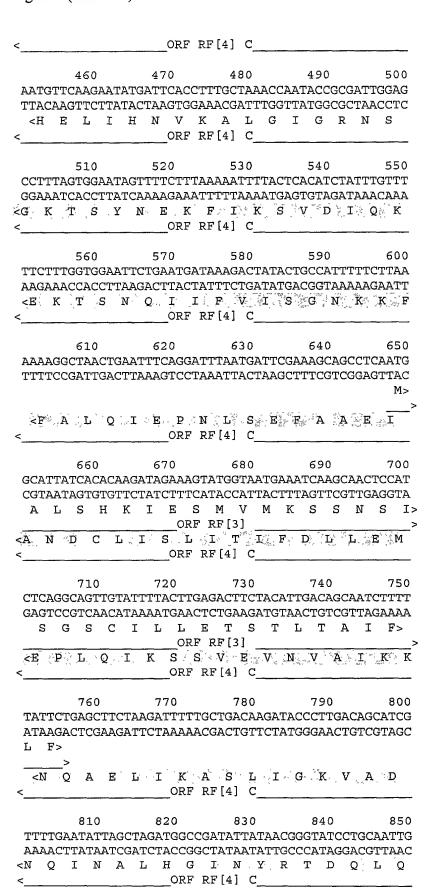


Title: Signal Peptides, Nucleic Acid Molecules and Methods for

Treatment of Caries 09/833,017

Sheet 10 of 19

Figure 9 (cont'd - 1)



Atty's Docket No. 1889-00401

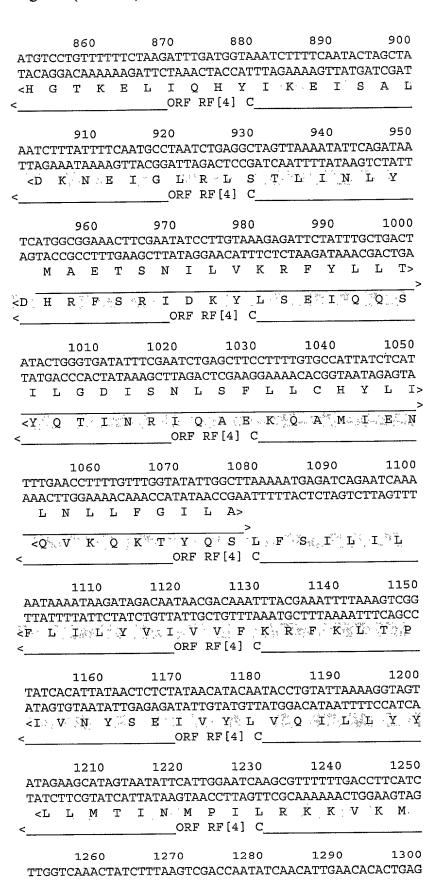
Applicants: Dennis CVITKOVITCH, et al.

Title: Signal Peptides, Nucleic Acid Molecules and Methods for

Treatment of Caries 09/833,017

Sheet 11 of 19

Figure 9 (cont'd - 2)



Atty's Docket No. 1889-00401
Applicants: Dennis CVITKOVITCH, et al.
Title: Signal Peptides, Nucleic Acid Molecules and Methods for Treatment of Caries 09/833,017
Sheet 12 of 19

Figure 9 (cont'd - 3)

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JAAA K ATAG ATC <l< td=""><td>AA(TT)</td><td>GCT S 166 CGG GCC</td><td>ATT  O  TTA  AAT</td><td>AGAT CCTA</td><td>V 16 FAAG ATTC</td><td>N ORI 570 STTA</td><td>TA ATA ATA L</td><td>F [4 1 AAC TTG G</td><td>] 68 CA GT</td><td>C_ 0 TT AA N</td><td>TG/ AC'</td><td>AAA TTT L</td><td>L 169 GTA</td><td> O Q T.A. T.A.</td><td>F CA' GT. M</td><td>L TTA AA:</td><td>[``` \AA( TT(</td><td>L 170 GGO CCO</td><td>F OO CT GA</td></l<>	AA(TT)	GCT S 166 CGG GCC	ATT  O  TTA  AAT	AGAT CCTA	V 16 FAAG ATTC	N ORI 570 STTA	TA ATA ATA L	F [4 1 AAC TTG G	] 68 CA GT	C_ 0 TT AA N	TG/ AC'	AAA TTT L	L 169 GTA	 O Q T.A. T.A.	F CA' GT. M	L TTA AA:	[``` \AA( TT(	L 170 GGO CCO	F OO CT GA

Title: Signal Peptides, Nucleic Acid Molecules and Methods for

Treatment of Caries 09/833,017

Sheet 13 of 19

Figure 9 (cont'd - 4)

TCATTCATTTTGCTCTCCTTTGATCAGCAATCACAGCTCTCAGTTTTGTT AGTAAGTAAAACGAGAGGAAACTAGTCGTTAGTGTCGAGAGTCAAAACAA <E N M KARRQDAIVARLKT ORF RF[5] C 1760 1770 1780 1790 1800 AACTTAGTTCGTGAAATAAGACAAGACTTATTATTTCGAAAATAGGCCAA TTGAATCAAGCACTTTATTCTGTTCTGAATAATAAAGCTTTTATCCGGTT <L K T R S I L C S K N N R F Y A L ORF RF[5] C 1810 1820 1830 1840 1850 GCGTTTTTTCCGATCAATACGGGTAATATTGGCAGGATTGACAATAAAAG CGCAAAAAAGGCTAGTTATGCCCATTATAACCGTCCTAACTGTTATTTTC  $<\!R-K-K-R^*\cdot D^*\cdot I_*\cdot R_*\cdot I_*\cdot I_*\cdot N-A^*\cdot P^*\cdot N-V\cdot I_*\cdot F_*\cdot S$ ORF RF[5] C 1870 1880 1890 MALKKSLIHFNNVSH> ORF RF[1] Q F L R K D M K V I D T ORF RF[5] C\_\_\_\_ <V 1920 1910 1930 1940 CTGCCGTAGAATTCAATCCGTTCATCATAAGTATAAAGGCAGAGCTTATG GACGGCATCTTAAGTTAGGCAAGTAGTATTCATATTTCCGTCTCGAATAC TAVEFNPFIISIKAEL M> ORF RF[1] <S G Y F E L R E T T Y L C L K H ORF RF[5] C <A T S N L G N M M L I F A S</pre> ORF RF[6] C 1960 1970 1980 1990 2000 GGCTGTTGAAGATGTTTCAAAATACAGAATCTCAGCAAAAGGGACCTGAA CCGACAACTTCTACAAAGTTTTATGTCTTAGAGTCGTTTTCCCTGGACTT S TELL FOR THE FOR THE FOR THE POWER ORF RF[5] C QLHKLICFRLLLSRF ORF RF[6] C 2020 2030 2040 ACTGAGTTTCAGATGAATGGAAAATAAAAAGTTCCTCTGATTGACCATTC TGACTCAAAGTCTACTTACCTTTTATTTTTCAAGGAGACTAACTGGTAAG <Q T E S S H F I F L E E S Q G N ORF RF[5] C <S L K L H I S F L F N R Q N V M R</pre> ORF RF[6] C\_\_\_

Atty's Docket No. 1889-00401
Applicants: Dennis CVITKOVITCH, et al.
Title: Signal Peptides, Nucleic Acid Molecules and Methods for Treatment of Caries 09/833,017

Sheet 14 of 19

Figure 9 (cont'd - 5)

2	060	2070	2080	2090	2100
		ATAGCATAAT			
AAGACCG	ACAAAAGG'	TATCGTATTA	IGTCGCGACT:	AAGTTACGCC	CACCCT
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		TTTCTAAAT			
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		TTTGATTTCA.			
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2	310	2320	2330	2340	2350
		TAGCGTCAAT.			
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2	410	2420	2430	2440	2450

Atty's Docket No.

1889-00401

Applicants: Dennis CVITKOVITCH, et al.

e: Signal Peptides, Nucleic Acid Molecules and Methods for

Treatment of Caries 09/833,017

Sheet 15 of 19

Figure 9 (cont'd - 6)

GGTTTCAAGACGTCCTTGTTGTAAAAAATCATCTTCCAATACAAAAATAG
CCAAAGTTCTGCAGGAACAACATTTTTTAGTAGAAGGTTATGTTTTATC
G F K T S L L>

V S R R P C C K K S S S N T K I>

<T E L R G Q Q L F D D E L V F I S
ORF RF[5] C

2460 2470 2480 2490 2500
AAATCATTATTTCTCCTTTAATCTTCTATTTAGGTTAGCTGATTAACACT
TTTAGTAATAAAGAGGAAATTAGAAGATAAATCCAATCGACTAATTGTGA
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AATAACC TTATTGG  Atty's Docket No. 1889-00401 Applicants: Dennis CVITKOVITCH, et al.

Title: Signal Peptides, Nucleic Acid Molecules and Methods for

Treatment of Caries 09/833,017

Sheet 16 of 19

## Figure 10

#### Α.

B.
MEEDFEIVFNKVKPIVWKLSRYYFIKMWTREDWQQEGMLILHQLLREHPELEEDDTKLY
IYFKTRFSNYIKDVLRQQESQKRRFNRMSYEEVGEIEHCLSSGGMQLDEYILFRDSLLA
YKQGLSTEKQELFERLVAGEHFLGRQSMLKDLRKKLSDFKEK

C.

Title: Signal Peptides, Nucleic Acid Molecules and Methods for

Treatment of Caries 09/833,017

Sheet 17 of 19

# Figure 11

A.

ATGAAACAAGTTATTTATGTTGTTTTAATCGTCATAGCCGTTAACATTCTCTTAGAGAT TATCAAAAGAGTAACAAAAAGGGGAGGGACAGTTTCGTCATCTAATCCTTTACCAGATG GGCAGTCTAAGTTGTTTTGGCGCAGACATTATAAGCTAGTACCTCAGATTGATACCAGA GACTGTGGGCCGGCAGTGCTGGCATCTGTTGCAAAGCATTACGGATCTAATTACTCTAT CGCTTATCTGCGGGAACTCTCAAAGACTAACAAGCAGGGAACAACAGCTCTTGGCATTG TTGAAGCTGCTAAAAAGTTAGGCTTTGAAACACGCTCTATCAAGGCGGATATGACGCTT TTTGATTATAATGATTTGACCTATCCTTTTATCGTCCATGTGATTAAAGGAAAACGTCT GCAGCATTATTATGTCGTCTATGGCAGCCAGAATAATCAGCTGATTATTGGAGATCCTG ATCCTTCAGTTAAGGTGACTAGGATGAGTAAGGAACGCTTTCAATCAGAGTGGACAGGC CTTGCAATTTTCCTAGCTCCTCAGCCTAACTATAAGCCTCATAAAGGTGAAAAAATGG TTTGTCTAATTTCTTCCCGTTGATCTTTAAGCAGAAAGCTTTGATGACTTATATTATCA TAGCTAGCTTGATTGTGACGCTCATTGATATTGTCGGATCATACTATCTCCAAGGAATA TTGGACGAGTACATTCCTGATCAGCTGATTTCAACTTTAGGAATGATTACGATTGGTCT GATAATAACCTATATTATCCAGCAGGTCATGGCTTTTGCAAAAGAATACCTCTTGGCCG TACTCAGTTTGCGTTTAGTCATTGATGTTATCCTGTCTTATATCAAACATATTTTTACG CTTCCTATGTCTTTCTTTGCGACAAGGCGAACAGGAGAAATCACGTCTCGTTTTACAGA TGCCAATCAGATTATTGATGCTGTAGCGTCAACCATCTTTTCAATCTTTTTAGATATGA ACCTTGCTCTCCATTCCGATTTATGCCATCATTATTTTTTGCTTTCTTGAAACCCTTTGA GAAAATGAATCACGAAGTGATGGAAAGCAATGCTGTGGTAAGTTCTTCTATCATTGAAG ATATCAATGGGATGGAAACCATTAAATCACTCACAAGTGAGTCCGCTCGTTATCAAAAC ATTGATAGTGAATTTGTTGATTATTTGGAGAAAAACTTTAAGCTACAAGTATAGTGC CATTCAAACCGCATTAAAAAGCGGTGCTAAGCTTATCCTCAATGTTGTCATTCTCTGGT ATGGCTCTCGTCTAGTTATGGATAATAAAATCTCAGTTGGTCAGCTTATCACCTTTAAT GCTTTGCTGTCTTATTTCTCAAATCCAATTGAAAATATTATCAATCTGCAATCCAAACT GCAGTCAGCTCGCGTTGCCAATACACGTCTTAATGAGGTCTATCTTGTCGAATCTGAAT TTGAAAAAGACGCCGATTTATCAGAAAATAGCTTTTTAGATGGTGATATTTCGTTTGAA AATCTTTCTTATAAATATGGATTTGGGCGAGATACCTTATCAGATATTAATTTATCAAT CAAAAAAGGCTCCAAGGTCAGTCTAGTTGGAGCCAGTGGTTCTGGTAAAACAACTTTGG CTAAACTGATTGTCAATTTCTACGAGCCTAACAAGGGGATTGTTCGAATCAATGGCAAT GATTTAAAAGTTATTGATAAGACAGCTTTGCGGCGGCATATTAGCTATTTGCCGCAACA GGCCTATGTTTTTAGTGGCTCTATTATGGATAATCTCGTTTTAGGAGCTAAAGAAGGAA CGAGTCAGGAAGACATTATTCGTGCTTGTGAAATTGCTGAAATCCGCTCGGACATTGAA CAAATGCCTCAGGGCTATCAGACAGAGTTATCAGATGGTGCCGGTATTTCTGGCGGTCA AAAACAGCGGATTGCTTTAGCTAGGGCCTTATTAACACAGGCACCGGTTTTGATTCTGG ATGAAGCCACCAGCAGTCTTGATATTTTGACAGAAAAGAAAATTATCAGCAATCTCTTA CAGATGACGGAGAAAACAATAATTTTTGTTGCCCACCGCTTAAGCATTTCACAGCGTAC TGACGAAGTCATTGTCATGGATCAGGGAAAAATTGTTGAACAAGGCACTCATAAGGAAC TTTTAGCTAAGCAAGGTTTCTATTATAACCTGTTTAAT

Title: Signal Peptides, Nucleic Acid Molecules and Methods for

Treatment of Caries 09/833,017

Sheet 18 of 19

Figure 11 (cont'd)

B.

MKQVIYVVLIVIAVNILLEIIKRVTKRGGTVSSSNPLPDGQSKLFWRRHYKLVPQIDTR
DCGPAVLASVAKHYGSNYSIAYLRELSKTNKQGTTALGIVEAAKKLGFETRSIKADMTL
FDYNDLTYPFIVHVIKGKRLQHYYVVYGSQNNQLIIGDPDPSVKVTRMSKERFQSEWTG
LAIFLAPQPNYKPHKGEKNGLSNFFPLIFKQKALMTYIIIASLIVTLIDIVGSYYLQGI
LDEYIPDQLISTLGMITIGLIITYIIQQVMAFAKEYLLAVLSLRLVIDVILSYIKHIFT
LPMSFFATRRTGEITSRFTDANQIIDAVASTIFSIFLDMTMVILVGGVLLAQNNNLFFL
TLLSIPIYAIIIFAFLKPFEKMNHEVMESNAVVSSSIIEDINGMETIKSLTSESARYQN
IDSEFVDYLEKNFKLHKYSAIQTALKSGAKLILNVVILWYGSRLVMDNKISVGQLITFN
ALLSYFSNPIENIINLQSKLQSARVANTRLNEVYLVESEFEKDGDLSENSFLDGDISFE
NLSYKYGFGRDTLSDINLSIKKGSKVSLVGASGSGKTTLAKLIVNFYEPNKGIVRINGN
DLKVIDKTALRRHISYLPQQAYVFSGSIMDNLVLGAKEGTSQEDIIRACEIAEIRSDIE
QMPQGYQTELSDGAGISGGQKQRIALARALLTQAPVLILDEATSSLDILTEKKIISNLL
QMTEKTIIFVAHRLSISQRTDEVIVMDQGKIVEQGTHKELLAKQGFYYNLFN

C.

ATGGATCCTAAATTTTTACAAAGTGCAGAATTTTATAGGAGACGCTATCATAATTTTGC  ${\tt GACACTATTAATTGTTCCTTTGGTCTGCTTGATTATCTTCTTGGTCATATTCCTTTGTT}$ TTGCTAAAAAAGAAATTACAGTGATTTCTACTGGTGAAGTTGCACCAACAAAGGTTGTA GATGTTATCCAATCTTACAGTGACAGTTCAATCATTAAAAATAATTTAGATAATAATGC AGCTGTTGAGAAGGGAGACGTTTTAATTGAATATTCAGAAAATGCCAGTCCAAACCGTC AAACACCAAAAGAGAAAAAGAAGAAGATCTAAGAGCAAGAAAGCTTCCAAAGATAA GAAAAAGAAATCGAAAGACAAGGAAAGCAGCTCTGACGATGAAAATGAGACAAAAAAGG  ${\tt TTTCGATTTTTGCTTCAGAAGATGGTATTATTCATACCAATCCCAAATATGATGGTGCC}$ AATATTATTCCGAAGCAAACCGAGATTGCTCAAATCTATCCTGATATTCAAAAAACAAG AAAAGTGTTAATCACCTATTATGCTTCTTCTGATGATGTTGTTTCTATGAAAAAGGGGC AAACCGCTCGTCTTTCCTTGGAAAAAAAGGGAAATGACAAGGTTGTTATTGAAGGAAAA ATTAACAATGTCGCTTCATCAGCAACTACTACTAAAAAAGGAAATCTCTTTAAGGTTAC TGCCAAAGTAAAGGTTTCTAAGAAAAATAGCAAACTCATCAAGTATGGTATGACAGGCA AGACAGTCACTGTCATTGATAAAAAGACTTATTTTGATTATTTCAAAGATAAATTACTG CATAAAATGGATAAT

D.

MDPKFLQSAEFYRRRYHNFATLLIVPLVCLIIFLVIFLCFAKKEITVISTGEVAPTKVV DVIQSYSDSSIIKNNLDNNAAVEKGDVLIEYSENASPNRQTEQKNIIKERQKREEKEKK KHQKSKKKKKSKSKKASKDKKKKSKDKESSSDDENETKKVSIFASEDGIIHTNPKYDGA NIIPKQTEIAQIYPDIQKTRKVLITYYASSDDVVSMKKGQTARLSLEKKGNDKVVIEGK INNVASSATTTKKGNLFKVTAKVKVSKKNSKLIKYGMTGKTVTVIDKKTYFDYFKDKLL HKMDN

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Title: Signal Peptides, Nucleic Acid Molecules and Methods for

Treatment of Caries 09/833,017

Sheet 19 of 19

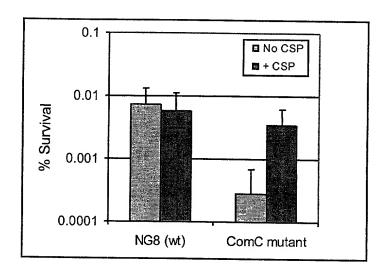


Figure 12